

Gastric electrical stimulation is an effective and safe treatment for medically refractory gastroparesis

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Background. *Gastroparesis is characterized by delayed gastric emptying in the absence of obstruction. Common symptoms include nausea, vomiting, and abdominal pain. Severe gastroparesis can result in recurrent hospitalizations, malnutrition, and even death. Gastric electrical stimulation (GES) is a low morbidity treatment that may be effective in patients who are refractory to medical therapy.*

Methods. *For a period of more than 35 months, 19 GES systems were implanted laparoscopically for refractory gastroparesis of diabetic (DG, n = 10), idiopathic (IG, n = 6), or postsurgical (PSG, n = 3) etiology. Total gastroparesis symptom scores (TSS) and weekly vomiting frequency were assessed. Gastric emptying studies were attained preoperatively and after 6 months.*

Results. *Mean follow-up was 38 weeks. There were no major complications. Within 6 weeks, frequency of vomiting decreased in 75% of DG (6/8) and 100% of IG (4/4) patients. No PSG patient complained of vomiting preoperatively. Mean TSS scores improved significantly at all intervals out to 1 year. Gastric emptying studies normalized in 80% of DG patients but in only 1 of the 6 patients with gastroparesis due to other causes.*

Conclusion. *GES therapy can lead to improvement in symptoms of gastroparesis and frequency of vomiting within 6 weeks. This therapy is a low morbidity treatment option that may help patients whose symptoms fail to improve with medical therapy. (Surgery 2008;144:566-74.)*

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GASTROPARESIS is a potentially debilitating disease. It is characterized by delayed gastric emptying in the absence of mechanical obstruction. Symptoms of gastroparesis are variable and may include early satiety, nausea, vomiting, bloating, and upper abdominal discomfort. Severe gastroparesis can result in significantly impaired quality of life, recurrent hospitalizations, malnutrition, and even death. The true prevalence of gastroparesis is not known. Although delayed gastric emptying is common in diabetics (up to 50% in some studies),¹ the true incidence of symptomatic gastroparesis is probably much lower.² The prevalence of gastroparesis may be increasing in recent years. Hospitalizations for gastroparesis symptoms and complications have increased dramatically. In 1995, 3,977 hospitalizations

in the United States were for the primary diagnosis of gastroparesis. By 2004, gastroparesis was the primary diagnosis for 10,252 hospitalizations.³

Gastroparesis literally means “paralyzed stomach.” Nearly any disease process that interferes with the neuromuscular function of the stomach can cause gastroparesis. The 2 most common causes are diabetes and idiopathic. In 1 published study that took place over a 6-year period, 146 patients with gastroparesis were evaluated; 82% of the patients were female, and the average age of symptom onset was 33.7 years. The etiologies for gastroparesis in this cohort of patients were as follows: idiopathic (36%), diabetic (29%), related to previous gastric surgery (13%), Parkinson’s disease (7.5%), collagen vascular disorders (4.8%), intestinal pseudo-obstruction (4.1%), and miscellaneous causes (6%).⁴

The medical management of gastroparesis consists of dietary modifications (frequent, small, low-fat meals) and prokinetic motility agents. Metoclopramide and erythromycin are the 2 most commonly prescribed drugs indicated for the treatment of symptomatic gastroparesis. Unfortunately, these medications are not uniformly tolerated or

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effective.^{5,6} Historically, surgical options for medically refractory gastroparesis have included feeding jejunostomy tubes, decompressing gastrostomy tubes, pyloroplasty, and gastrectomy. These procedures are invasive, associated with significant potential morbidity, and often do not result in patients resuming oral intake without severe symptoms.⁷ Recently, a new surgical treatment option for medically refractory gastroparesis was introduced. Gastric electrical stimulation (GES) with high frequency (12 cycles per minute) and low energy (pulse width of 300 μ s) has been shown to lead to reduced gastroparesis symptoms and improved quality of life in those with medically refractory gastroparesis symptoms.^{8,9} An implantable gastric electrical stimulator (Enterra Therapy; Medtronic, Minneapolis, Minn) received a Humanitarian Device Exemption from the Food and Drug Administration (FDA) in 1999. Gastric-stimulating electrodes can be implanted laparoscopically with minimal morbidity, making GES an attractive alternative to other surgical procedures for gastroparesis.¹⁰

METHODS

Between October 2005 and August 2007, a total of 19 GES systems were implanted at the University of Wisconsin Hospital and Clinics. All patients suffered from medically refractory gastroparesis. Delayed gastric emptying was confirmed in all cases with a nuclear medicine gastric emptying study. Gastric electrodes were implanted in all cases with either laparoscopic or minimally invasive robotic techniques by a single surgeon (J.G.).

For robotic cases, a diagnostic endoscopy is performed early in the case, and the endoscope is left in the patient's esophagus. After port placement, the bedside robotic cart is docked to the patient. Diagnostic endoscopy to confirm lead placement in robotic cases can be quite difficult unless the endoscope is preplaced in the esophagus. For all cases, a disposable ruler is trimmed to exactly 10-cm by 1-cm and inserted into the abdomen. The pylorus is identified, using endoscopy to confirm the correct location if necessary, and a point exactly 10-cm proximal to the pylorus on the greater curve of the gastric antrum is marked with electrocautery. Another mark 10-cm proximal to the pylorus and 1-cm toward the lesser curve from the first mark is made with electrocautery. The 2 GES electrodes are placed in these precisely marked locations.

It is important that the ski needles attached to the electrodes are tunneled and parallel in the seromuscular anterior gastric wall for approximately 2 cm. Electrode placement is first checked

with diagnostic endoscopy to confirm that the electrodes have not perforated the mucosa into the gastric lumen. Ski needles identified endoscopically are repositioned until properly placed. Once positioned, electrodes are anchored in the gastric wall by passing the ski needles through distal anchoring discs. Sutures are used to anchor each electrode to the anterior wall of the stomach at both the proximal and distal anchoring discs for each lead. Once secured, proper electrode placement is confirmed by externalizing the proximal end of each lead, connecting each lead to the neurostimulator generator, and checking to see if the impedance of the circuit created by the GES system and stomach between the leads is in the desired therapeutic range of 200 to 800 Ω . To complete the case, the generator is implanted subcutaneously and the system is programmed and activated. Feeding jejunostomy tubes were laparoscopically placed during operation to initiate GES when clinically indicated.

Our standard clinical protocol calls for follow-up visits at 2 weeks, 6 weeks, 6 months, and annually for all patients. Between standard visits, patients are seen every 4 to 6 weeks if symptoms have not improved for adjustments to the GES parameters according to a published adjustment algorithm.¹¹ All postoperative visits and stimulator adjustments were performed by a single nurse practitioner (G.B.). Symptom response is assessed objectively using a total gastroparesis symptom score (TSS) questionnaire at each clinical encounter. The TSS instrument has been used to evaluate efficacy in numerous GES series, including the clinical trial that led to the FDA approval for this particular device.⁹ Although the TSS itself has not undergone a rigorous evaluation and validation process, 5 of the 6 items are similar to items included in the 9-question Gastroparesis Cardinal Symptom Index (GCSI). The GCSI has been demonstrated in studies to be a reliable and valid instrument for measuring the symptom severity in gastroparesis.¹²

To derive a TSS score, patients were asked to rate the severity of 6 common gastroparesis symptoms (vomiting, nausea, early satiety, bloating, after-meal fullness, and epigastric pain) on a 5-point Likert scale. The maximum TSS score was 24 for those patients with the most severe symptoms, and the least possible score was 0. For this study, a TSS score consistently 3 points or more lower than the preoperative score was considered an improvement. Patients who failed to experience at least a 3-point decrease in TSS scores were considered to have failed GES therapy after 12 months.

Weekly frequency of vomiting was recorded during each encounter (0, 1, 2–3, 4–6, >7 times per week). Overall quality of life and health was assessed with the Short Form 36 (SF-36) quality of life instrument preoperatively and at 6 months postoperatively. The SF-36 is a survey of health and quality of life encompassing scaled scores in 8 domains: (1) vitality, (2) physical functioning, (3) bodily pain, (4) general health perceptions, (5) role physical, (6) role emotional, (7) role mental, and (8) mental health. Each scale is directly transformed into a scale from 0 (worst) to 100 (best) on the assumption that each question carries equal weight. The SF-36 has been extensively validated. Nuclear medicine gastric emptying studies were repeated after 6 months of GES. Data were collected prospectively and reviewed retrospectively. Preoperative TSS and SF-36 scores were compared to all postoperative intervals using the Wilcoxon signed-rank test. Data were tested for a normal distribution using a Shapiro-Wilk test.

RESULTS

A total of 19 patients underwent surgery to initiate GES. The cause of gastroparesis was diabetes (DG) in 10, idiopathic (IG) in 6, and postsurgical (PSG) in 3. The 3 patients in the PSG group had antireflux surgery previously. The status of the vagus nerve at the time of operation to initiate GES was unknown. Of the 3 patients with presumed PSG, 2 had significant symptoms of severe bloating prior to fundoplication, and delayed gastric emptying may have been a preexisting condition. In the third PSG patient, gastroparesis symptoms did not occur for many years after a successful fundoplication, again raising the possibility that the delayed gastric emptying may have been secondary to a cause other than vagus nerve injury incurred at the time of antireflux surgery.

Mean follow-up after surgery was 38 weeks (42 weeks DG, 21 weeks IG, 64 weeks PSG, PSG vs IG; $P = .02$, other comparisons were not significant). The range for follow-up was 4 weeks to 35 months. For the entire case series, 14 patients were female (73%): 6 DG (60%), 6 IG (100%), and 2 PSG (66%). The mean age at the time of operation was 49 years (52 DG, 38 IG, 57 PSG; age differences between groups were not significant). The average duration of symptoms prior to the initiation of GES was 8.2 years. All devices were successfully implanted laparoscopically or robotically without conversions to an open procedure. Mean operating room time was 146 ± 41 minutes. Mean length of stay after surgery was 1.8 ± 1.4 days.

Table I. Mean and standard deviation total gastroparesis symptom scores (TSS) before and after the initiation of gastric electrical stimulation therapy—all patients

	TSS (n = 19)	P value vs preop
preop	17.1 \pm 4.7	–
6-wk postop	7.9 \pm 6.4 (16)	.0006*
6-mo postop	7.6 \pm 5.6 (11)	.01*
12-mo postop	7.7 \pm 6.8 (9)	.01*

preop, Preoperative; postop, postoperative.
* $P < .05$.

There were no early complications and one late complication during the time period of this study. The late complication was in a PSG patient with abdominal wall pain at the site of the neurostimulator generator, which required surgical repositioning. Her pain improved after this intervention. Feeding jejunostomy tubes were placed in 2 patients, 1 with IG and 1 with DG. Both of these patients were able to resume oral intake, and both feeding tubes were removed between 6 and 8 weeks postoperatively. One patient with a 56-year history of type 1 diabetes mellitus and DG died 4 months postoperatively from what was presumed to be a cardiac event. No autopsy was performed.

TSS scores demonstrate marked improvement compared to preoperative values (Table I). When TSS scores are evaluated based on indication, DG patients demonstrate improvements at all evaluated time intervals (Table II). Of the 6 symptoms assessed by the TSS, all demonstrated some degree of improvement for the average patient. Of patients with DG, 8 of 9 rated their gastroparesis symptoms as improved within the first 6 weeks postoperatively. For IG patients, 3 of 4 patients felt that their symptoms had improved in this interval. In PSG patients, 2 of 3 noted an improvement in the first 6 weeks. Of the 9 patients with 1 year follow-up data, 2 (22%, 1 IG and 1 PSG) failed to realize an improvement as measured by the TSS. In these 2 patients, 1 device has been turned off and left in situ at the patient's request, and 1 device is still active.

Prior to the initiation of GES, weekly vomiting frequency was ≥ 4 episodes per week in 8 of 10 DG, 4 of 6 IG, and 0 of 3 PSG patients. Within 6 weeks, weekly vomiting frequency had significantly decreased for those with frequent vomiting preoperatively in 75% of DG (6/8) and 100% of IG (4/4) patients. This decrease in frequency of vomiting was maintained during all postoperative evaluations.

Table II. Mean (and standard deviation) total gastroparesis symptom scores (TSS) prior to and following the initiation of gastric electrical stimulation therapy by etiology

	DG (n = 10)	IG (n = 6)	PSG (n = 3)
TSS preop	16.9 ± 5.5	17.8 ± 3.9	16 ± 4.6
TSS 6 wk postop	7.1 ± 7.5 (9)*	9.8 ± 3.9 (4)	7.7 ± 6.7 (3)
TSS 6-mo postop	6.6 ± 7 (5)*	9 ± 6 (3)	8 ± 4.4 (3)*
TSS 12-mo postop	5.6 ± 7.4 (5)*	14 ± 6.8 (2)	6.5 ± 6.4 (2)

DG, Diabetic gastroparesis; IG, idiopathic gastroparesis; PSG, postsurgical gastroparesis; *preop*, preoperative; *postop*, postoperative.

* $P < .05$ for comparisons to mean preoperative scores based on etiology.

Gastric emptying times as determined by nuclear medicine gastric emptying studies normalized in 4 of 5 (80%) patients with DG and in 1 (a patient with PSG) of 6 patients with other causes for their gastroparesis after 6 months of therapy. For DG patients with 6-month follow-up gastric emptying studies, the mean gastric half-emptying time (T-1/2) prior to GES was 318 ± 206 minutes. This decreased to a mean gastric emptying time of 135 ± 95 minutes for these 5 patients after 6 months ($P = .05$). These same calculations were difficult to derive for the remaining patients because 3 of 6 patients with 6-month follow-up studies had essentially 0% emptying at 120 minutes prior to GES. Mean TSS scores at 6 months did not differ for those patients whose gastric emptying times had normalized compared to those who still had delayed gastric emptying (normal gastric emptying time TSS score = 8.4 ± 6.7 vs delayed gastric emptying TSS score = 7.0 ± 5.2 ; $P = 0.6$).

Quality of life as measured by the SF-36 did not change. SF-36 scores were compared before operation ($n = 20$), after 6 months ($n = 10$), and after 1 year ($n = 8$). Among the 8 domains measured with this instrument, only "bodily pain" improved (preoperative 34.9 vs 6 months 42.7; $P = .04$) and only at the 6-month interval. Due to the small sample size, it is possible that a clinically significant difference in health and quality of life may not have been detected if it exists. Patients' reported health improved by 6 months postoperatively compared to prior to surgery (2.1 vs 4.0 on a 5-point Likert scale; $P = .002$).

DISCUSSION

In our experience, GES has proven to be a safe and effective treatment for gastroparesis symptoms. Gastroparesis symptoms and vomiting frequency improved in a high proportion of patients within 6 weeks of therapy, and the results have been durable out to 1 year in a small subset. Two patients with significant malnutrition were able to resume adequate oral intake and discontinue

supplemental enteral feedings within 2 months of therapy. All of this was accomplished in a group of patients who had failed to respond to noninvasive treatment of their symptoms, without major morbidity.

Traditional surgical options for patients with significant medically refractory gastroparesis include gastrostomy/jejunostomy tubes, total parenteral nutrition, and gastrectomy or surgical drainage procedures. In refractory patients with severe nausea and vomiting, placement of a gastrostomy tube for intermittent decompression may help to provide some symptom relief. In 1 series, symptoms were decreased, patients gained weight, and 6 of 8 patients studied were able to return to work or school with a venting gastrostomy.¹³ Jejunostomy tubes in patients unable to maintain nutrition with oral intake can improve nutrition, decrease symptoms, and decrease hospitalizations.¹⁴ Some patients with small-bowel dysmotility may be unable to tolerate jejunostomy tube feedings, and chronic parenteral nutrition becomes necessary. This approach can be costly and is associated with significant morbidity including infections and liver disease. There are limited controlled data regarding gastrectomies and gastric drainage procedures for the treatment of diabetic and idiopathic gastroparesis.

A recent systematic review of surgical treatment for gastroparesis uncovered 4 reviewable studies consisting of a total of 12 patients.⁸ These were retrospective reviews of small, uncontrolled case series. Symptomatic outcomes in all 4 studies were assessed subjectively, and most patients reported feeling better after the operative treatment. A more recent series of 7 patients to undergo subtotal gastrectomy for diabetic gastroparesis demonstrated that 6 of 7 patients experienced relief of vomiting almost immediately and out to 6 years after operation in some cases.¹⁵ Unfortunately, 3 patients developed renal failure and 2 patients died within 5 months of operation.

Operative interventions for postsurgical gastroparesis may be a viable option for carefully selected

patients. A number of relatively small, uncontrolled case series and retrospective reviews have been published regarding the outcomes of subtotal gastrectomy and completion gastrectomy for refractory postsurgical gastroparesis. Symptom improvement is reported in 67% to 100% of patients.⁸ In 1 series that objectively evaluated symptomatic outcomes, patients with a preoperative grade of Visick III-IV improved in only 43% of cases.¹⁶ Clearly, the results of operative interventions for significant gastroparesis are difficult to predict based on available data and can be associated with significant patient morbidity. GES is a fundamentally different approach to refractory gastroparesis, and preliminary results have been encouraging.

The exact mechanism of action for GES is unknown. This device is often called a "gastric pacemaker." This terminology leads to the common misconception that the stomach is actually being paced and stimulated to empty by electrical energy. This is in fact not the case. True gastric pacing requires energy at a higher amplitude and lower frequency than is typically used for GES. In gastric pacing, the smooth muscle of the stomach is stimulated to entrain gastric slow waves and normalize myoelectric activity as well as gastric emptying.^{17,18} Substantive clinical or symptomatic benefit for gastric pacing has not been demonstrated. It is interesting that we observed such a high frequency of normalized gastric emptying times in our diabetic patients with GES, whereas very few patients with gastroparesis due to other causes experienced the same result. Our results are consistent with others who have determined that gastric emptying studies performed while a patient is on GES therapy have poor correlation with actual symptomatic outcomes.¹⁹

In GES, low-amplitude and high-frequency energy is delivered to the antrum of the stomach. Several potential mechanisms of effect for GES have been proposed. These hypotheses include a potential effect on the enteric nervous system, effects on the autonomic nervous system (such as vagal stimulation or adrenergic blockade), changes in gastric fundic tone, changes in antral motor function, and a direct central nervous system effect.²⁰ A direct central nervous system effect may involve the stimulation of a central nausea and vomiting center in the brain leading to symptomatic improvement. A study²² of patients with GES for 1 year examined the physiologic effects of therapy. Using electrocardiogram, gastric barostat measurement, and positron emission tomography brain imaging, investigators determined that a

significant increase in vagal and thalamic activity occurred. In addition, a significant increase in the discomfort threshold for both pressure and volume with gastric distention was demonstrated. This study suggests that symptomatic improvement following GES may be due to enhanced vagal autonomic function, decreased gastric sensitivity to distention, and the activation of central control mechanisms for nausea and vomiting through thalamic pathways.²¹

GES therapy has been shown to consistently lead to improved gastroparesis symptoms in patients with medically refractory gastroparesis in published series.^{10,22} Others have demonstrated that GES can lead to fewer gastroparesis-related hospitalizations,²³ improved nutritional parameters,²⁴ and better glycemic control with lower hemoglobin A1C levels in diabetics.^{25,26,27} The Worldwide Anti-Vomiting Electrical Stimulation Study trial (WAVESS) was a prospective, randomized, double-blinded, controlled trial evaluating GES safety and efficacy.⁹ Data from this study were the basis for the Humanitarian Device Exemption granted for this device by the FDA. In the WAVESS trial, neurostimulators were placed, and patients were randomized and blinded as to whether the device was on or off. After 6 months, patients crossed over and had their stimulators turned from off to on and vice versa. Arguing against a predominant placebo effect for GES, patients in this trial experienced a significant decrease in vomiting episodes and symptom scores, and clearly felt better when the devices were turned on than when they were turned off.

Although mean TSS scores improved significantly in our study, about 20% of our patients did not attain major symptomatic benefit. It has been suggested that conclusions regarding the efficacy of GES prior to 1 year may be premature, because it can sometimes take this long for certain patients to respond.¹² It is possible that, as our series matures, some patients with a poor initial response may improve with ongoing GES therapy and stimulation parameter adjustment. Predicting who is likely to benefit from GES and who is not has proven to be difficult. Reasons for treatment failure are likely to be multifactorial. Forster and colleagues²⁹ demonstrated that some patients with gastroparesis are lacking the interstitial cells of Cajal from their stomachs on full-thickness biopsy. The interstitial cells of Cajal are thought to be the "pacemaker cells of the stomach," responsible for initiating the spontaneous gastric contractions that occur between meals. Patients without interstitial cells of Cajal were found to have a higher

symptomatic failure rate with GES.²⁸ Others have determined treatment failure rates according to indication. In 1 study, patients with both diabetic (21% failure rate) and postsurgical (16% failure rate) gastroparesis fared better than those with idiopathic gastroparesis (35% failure rate).²⁹

The 2 most common indications for GES are diabetic and idiopathic gastroparesis. Several published series, including the current study, include patients with postsurgical gastroparesis who have done well with GES.³⁰ Postsurgical gastroparesis is most often a consequence of peptic ulcer surgery, usually with the concurrent performance of vagotomy where the risk may be as high as 5%.³¹ Gastroparesis may also occur after antireflux surgery, although the risk is much lower (<1%).³² Gastroesophageal reflux disease is associated with delayed gastric emptying in approximately 40% of patients.³³ Delayed gastric emptying may play a causative role in certain patients with gastroesophageal reflux disease. It is likely that some patients with gastroparesis diagnosed after a fundoplication may have actually had this condition present to some degree before surgery as well. Of the 3 postsurgical patients in the current series, 2 suffered from significant bloating before antireflux surgery. We did not conduct tests to evaluate the status of the vagus nerve before opting to offer these patients GES therapy. Although our numbers are small, gastroparesis symptoms in patients with a prior fundoplication did improve with GES.

Data regarding long-term results of GES are beginning to emerge. Lin's group²⁶ reported symptomatic results in 37 patients, all with greater than 3 years follow-up (mean, 45 months). After 3 years of therapy, all patients continued to derive major symptomatic benefit from GES.³⁴ More recently, a multiinstitutional study demonstrated that, of 156 patients followed for an average of 4 years, significant improvements in gastrointestinal symptoms and health-related quality of life were still present.¹⁰

CONCLUSION

GES for symptomatic and medically refractory gastroparesis is a safe and effective treatment option. Gastrointestinal symptoms related to gastroparesis and vomiting will significantly improve in the majority of cases. Many patients, especially diabetics, will have normal gastric emptying times on GES therapy, although normal gastric emptying does not seem to be necessary for a good symptomatic response. Gastric electrodes can be implanted using minimally invasive surgical techniques with

little morbidity. GES is the procedure of choice for patients with medically refractory gastroparesis symptoms.

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DISCUSSION

Dr Vic Velanovich (Detroit, Mich): Gastric neurostimulation represents a cusp in surgical history. It represents another transition of diseases that were nearly always treated medically but now can be treated surgically (or medically). Our increased understanding of neurophysiology has now added targeted electrical stimulation to the nervous system. This is truly a tipping point in the management of many disease processes and we are going to see more of this type of management.

Overall, Dr Gould's group has demonstrated a response rate of about 74% in 6 weeks, which is similar to my experience. And, considering the intractable nature of these patients' symptoms, this is a remarkable response rate. We should not lose sight of the fact that this is a difficult (and needy) group of patients, all of whom were nearly debilitated by their disease and at the end of their ropes.

I do have a few questions for the authors.

What do you consider an adequate preoperative workup? How do you rule out mechanical obstruction? Do you look for other potential diagnoses like diffuse autonomic nervous system dysfunction or cyclical vomiting syndrome? It has been my experience that referring physicians don't necessarily think of these alternative diagnoses.

Which patients would you advise against a neurostimulator? Specifically, I am asking about symptoms. It has been my experience that patients with nausea and vomiting, as you have shown, respond well, while those with pain and bloating don't. Therefore, I have gone away from implanting this device in patients whose symptoms are primarily pain and bloating.

How do you follow your patients? Do you do the follow-up and interrogate the device, or does a gastroenterologist do it? Do you make adjustments on the electric dosing or do you just "set it and forget it"?

Dr Jon C. Gould (Madison, Wis): Your first question had to do with the adequate preoperative workup. All patients obviously had gastric scintigraphy following gastric emptying. They all had endoscopies. Patients that are at risk for mechanical obstruction, those who had significant peptic ulcer disease, those with prior small bowel resections or obstructions will get an upper GI and small bowel follow through series.

With regard to alternative diagnoses like cyclical vomiting syndrome, I have actually turned down some people with cyclical vomiting syndrome who had normal gastric emptying times, and I am beginning to wonder whether that is the proper approach. As mentioned, the correction in gastric emptying couldn't correlate with the symptoms. And the mechanism for therapy, why this works, is not entirely clear to me. And I suspect it would also work in people with cyclical vomiting syndrome who would have normal gastric emptying. I also suspect that a lot of our idiopathic patients, patients labeled as having

idiopathic gastric emptying, may have a component of autonomic neuropathy as well.

With regard to contraindications based on symptoms, I agree. As we have collected data and as we have looked at symptoms specifically on a symptom-by-symptom basis, we have noticed that nausea and vomiting consistently improved whether the diagnosis is idiopathic gastroparesis or diabetic gastroparesis. All of our diabetic patients had either nausea or vomiting, and in those patients who had a component of epigastric pain and bloating, those other symptoms tend to get better with time, and fairly immediately as well.

What we have noticed, however, is that a number of our idiopathic patients did not have nausea or vomiting and did have a primary component of epigastric pain. They did not respond as well to therapy. In fact, in many of those folks, the pain did not get better, and this is where our failures come. So we have gotten to the point now where specifically for idiopathic gastroparesis, unless there has been a significant component of nausea and vomiting, we don't believe that they are going to benefit from the therapy.

How do we do follow-up? We have a nurse practitioner who runs the Enterra Therapy clinic and she programs these devices herself. Our programming philosophy is to increase the voltage of the electrical stimulation in increments and to leave most of the other stimulation parameters at their default settings. I think with time, as you alluded to, the longer duration of therapy, people do tend to improve. I think when you really start tinkering with this device and overmanaging it, you can actually sometimes make things worse.

We have noticed that certain gastroparesis symptoms respond to GES better than others. Patients with primarily pain and bloating often don't do well. We have also observed that people who are eventually going to go on to respond to this therapy feel somewhat better after only 6 weeks of treatment. In some cases, noticeable improvement may take as long as a year, but usually you get a sense on whether this is going to work much sooner than that.

Dr Mary Francis Otterson (Milwaukee, Wis): I also have some questions regarding objective criteria. For example, do you have data on the patient's weight and nutritional status?

Dr Jon C. Gould (Madison, Wis): We do have some data with regard to weights. We have demonstrated that patients who are losing weight prior to the initiation of therapy are able to gain weight. That is not always the case. Not everybody has lost a significant amount of weight beforehand. But those that are really challenged did benefit from the therapy and have been able to gain weight. Nutritional parameters have reflected that as well.

Dr Nathaniel Soper (Chicago, Ill): That was a fascinating study that you have done. Having spent several years with Keith Kelly trying to pace human stomachs, I am wondering what this is all about. We have proved essentially you can't pace most human stomachs. Very rarely

can you actually entrain it. And, as you said, this is different, this is stimulation. So my question to you is, what setting do you put the stimulator on usually? What kind of a fallback setting do you use? What do you think it is doing, and why do you think it works?

Dr Jon C. Gould (Madison, Wis): There is actually a kind of a default initial setting in regard to the on/off cycle duration and the frequency. What is going on? Again, I am not entirely certain. I think the mechanism of action here is central, I think this treatment is a lot more analogous to a neurostimulator placed in someone with chronic back pain than it is to a cardiac pacemaker placed in someone with a cardiac arrhythmia. So I think that we are actually affecting the central system that is responsible for patients proceeding on to nausea and vomiting and a lot of the other symptoms that go along with this, perhaps blocking that pathway or affecting it another way.

Dr Scott M. Wilhelm (Cleveland, Ohio): From your laparoscopic picture, this is on the greater curvature of the stomach where you are implanting about 10 cm away from the pylorus. I am curious if you have looked at different places of implantation or of doing highly selective vagotomies with the concept of protecting the nerve and lesser curvature of people so this is really nerve stimulation. Do you think that that has any relationship to your overall function and overall success of the procedure?

Dr Jon C. Gould: With regard to the placement, the goal here is to place these within 10 cm of the pylorus. And it was emphasized to me when I was learning this that this needed to be precise, needed to be exactly 1 cm apart and parallel. The area of implantation should be near where the migrating motor complex originates in the stomach.

Dr Norman C. Estes (Peoria, Ill): I make a small incision and then, through that pocket incision, just go on the end and pull the stomach out, because I have to do it as an outpatient. Medicare pays about, I think, \$14,000 for the DRG, and the pacemaker costs over \$10,000. So there is not much margin there. What is your experience with reimbursements for this?

Dr Jon C. Gould (Madison, Wis): As far as reimbursement goes, you are right, it depends on the payer. And margin is something I will need to take a look at here as we continue to do more of these, and especially as we start to use these expensive technologies like robotics.

Dr Michael S. Nussbaum (Cincinnati, Ohio): I think that a paper like this is very important; it establishes the effectiveness of this in that the reimbursement is variable. And with such low margins, although there are definitely studies that show that this is effective, many hospitals are unwilling to take on the extra cost. A lot of payers in this area don't reimburse even at that rate. And so we have had difficulty convincing our hospital administration to allow us to have these procedures here. How have you funded these patients? Or are they all covered to the point where your hospital administration

isn't looking at every one of these and giving you a hard time about doing these cases, particularly when you start adding expensive technology like laparoscopy and robotics on top of the pacer itself?

Dr Jon C. Gould (Madison, Wis): All these cases, with the exception of Medicare patients, had prior authorization. Sometimes that requires a bit of education

on my part with the insurance company. In fact, it is rare when I can send a letter out and get approval.

In terms of the margin and the bottom line reimbursement. I continue to do these operations using minimally invasive technologies and approaches. I have not yet had a conversation with my hospital administrators about this fact.